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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/809,158	03/15/2001	Carol O. Cowing	LANCELL.002CP1	5364

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/809,158	Applicant(s) Cowing
	Examiner Kar n Canella	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above, claim(s) *4, 5, 7, 9, 10, 37, and 42* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 6, 8, 11-16, 18, 23, 25-36, 38-41, and 43-57* is/are rejected.

7) ☒ Claim(s) *17, 19-22, and 24* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *2, 8*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Please note that the examiner assigned to this application has changed.

2. Acknowledgment is made of applicants election of species as required by Paper No. 6. Acknowledgment is also made of applicants election with traverse of Invention I. After review and reconsideration, the Restriction Requirement of Paper No. 5 is withdrawn; however, the election of species requirement of Paper No. 5 is maintained.

3. Claims 1-57 are pending. Claims 4, 5, 7, 9, 10, 37 and 42, drawn to non-elected species, are withdrawn from consideration. Claims 1-3, 6, 8-36, 38-41 and 43-57 are examined on the merits.

Claim Rejections - 35 USC § 112

4.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 12, 23, 45, 51, 52, 54 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite the limitation of a compound or molecule having a molecular weight of less than or equal to 500 Daltons. The claims are vague and indefinite in the recitation of a 500 Dalton protein in the absence of the specific method used to measure the molecular weight. It is well know in the art that proteins can display widely differing apparent molecular weights as a result of complex physical and chemical interactions with buffer and gel matrix constituents, therefore the actual method used to define the molecular weight is a necessary part of defining molecular weight.

Claim 23 is vague and indefinite because it is unclear how the introduction of the antigen or epitope thereof of "at least a portion" or the respiratory, urogenital or gastrointestinal tracts differs from the introduction of the antigen or epitope thereof to the respiratory, urogenital or gastrointestinal tracts.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 25, 26, 32-36, 38-41, 43-50 and 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims are drawn to methods for vaccinating a mammal comprising either transformation of a cell within a mammal (claims 25 and 26) or introducing into a mammal an expression vector for the expression of the antigen, or delivering into the mammal a nucleic acid vaccine comprising DNA or RNA encoding the antigen. Thus, the claims read on methods of gene therapy. The specification has not provided any specific examples of said gene therapy wherein a defined vector expressing a specific antigen was successfully used within the claimed method . Gene therapy is a highly unpredictable and undeveloped and clinical efficacy is unreliable. According or Orkin et al (Report and recommndation of the Panel to Assess the NIH Investment in research on Gene therapy, 1995, pp. 1-41) "significant problems remain in all basic aspects of gene therapy. Major difficulties at the basic level include shortcomings in all current gene transfer vectors and an inadequate understanding of the biological interaction of these vectors with the host". The specification fails to disclose the intended antigens to be expressed, the vectors or nucleic acids to be administered, what dosages would be considered therapeutically effective, the routes and methods of administration. The specification lacks any working examples that expression vectors, viral vectors or naked DNA would deliver the DNA encoding the antigens to the appropriate or intended sites and that the DNA once delivered would be expressed in sufficient quantities to effect the desired immune response. In view of the quantity of experimentation necessary to determine the above parameters, the lack of direction and guidance presented and the absence of working examples of in vivo gene therapy, the breath of the claims, drawn to any antigen, and the

unpredictable and undeveloped state of the art with respect to gene therapy, it would be undue experimentation, without reasonable expectation of success, for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
>
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

9. Claims 1-3, 6, 8, 11, 12, 13-16, and 28-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Marchal et al (Adv Exp Med Biol, 1995, Vol. 378, pp. 219-221). Claim 1 is drawn to a method for vaccinating a mammal against an antigen comprising introducing into the mammal an effective dose of the antigen or an epitope thereof; and administering to the mammal a topical treatment in an amount sufficient to increase the number of antigen-bearing denrdritic cells in a lymphoid organ, wherein introducing the antigen and administering the treatment are preformed independently in any order. Claim 2 embodies the method of claim 1 wherein the topical treatment comprises a lipophilic molecule capable of traversing the stratum corneum and

inducing immature dendritic cells to migrate to draining lymphoid organs. Claim 3, 6, 8 and 11 are drawn in part to the method of claim 2 wherein the lipophilic molecule is dibutylphthlate. Claim 12 embodies the method of claim 2 wherein the lipophilic molecule is less than or equal to 500 Daltons. Claim 13 embodies the method of claim 2 wherein the lipophilic molecule has an oil/water partition coefficient of greater than 1. Claim 14 embodies the method of claim 13 wherein the lipophilic molecule has an oil/water partition coefficient of between about 10 and about 10^6. Claim 15 embodies the method of claim 2 wherein the topical treatment further comprises an organic solvent. Claim 16 embodies the method of claim 15 wherein the organic solvent is acetone. Claim 28 is drawn to the method of claim 1 wherein the amount of topical treatment is sufficient to increase the number of antigen-bearing dendritic cells in the lymphoid organ by a factor of about 2 to about 1000 times the number of resident dendritic cells. Claim 29 embodies the method of claim 28 wherein the number of antigen-bearing dendritic cells in the lymphoid organ is increased by a factor of about 5 to about 1000 times the number of resident dendritic cells in an untreated mammal. Claim 30 embodies the method of claim 1 wherein the amount of topical treatment is further characterized as being sufficient to increase the local release of an endogenous inducer of dendritic cell migration and maturation. Claim 31 embodies the method of claim 1 wherein the amount of topical treatment is further characterized as being sufficient to alter the plasma membrane expression of an adhesion molecule.

Marchal et al disclose a method of topical immunization comprising the administration of FITC in a 50% acetone/dibutlphthalte solution. Marchal et al disclose that the immunization procedure was repeated. It is noted that the limitation of "introducing the antigen and administering the treatment are preformed independently in any order" does not exclude the simultaneous administration of both adjuvant and treatment. The recitation of the administration thus fulfills the specific embodiment of claim 52 drawn to a repeated topical application of a lipophilic compound and the administration of the acetone/dibutylphthalte solution fulfills the specific embodiments of claims 3, 6-8, 11-16. Further, although Marchal et al do not specifically teach the further embodiments of claims 28-31 they would be inherently within the method of Marchal et al.

10.. Claims 1, 2, 3, 7, 8, 11-15, 23, 28-31 and 55-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Gizurarson et al (WO 94/17827). The specific embodiments of claims 1, 2, 12-16 and 28-31 are recited above. It is noted that the limitation of "introducing the antigen and administering the treatment are preformed independently in any order" does not exclude the simultaneous administration of both adjuvant and treatment. Claim 11 is drawn in part to benzoic acid. Claim 23 embodies the method of claim 1 wherein the antigen is introduced into the mammal via delivery to the respiratory, urogenital or gastrointestinal tract. Claim 55 is drawn to a method for vaccinating a mammal against an antigen comprising providing the mammal with an effective dose of the antigen or an epitope thereof and administering internally to the mammal a treatment in an amount sufficient to increase the number of antigen-bearing dendritic cells in a lymphoid organ. Claim 56 embodies the method of claim 55 wherein the administration occurs via the gastrointestinal, respiratory or urogenital tract. Claim 57 embodies the method of claim 55 wherein the treatment comprises a lipophilic molecule with a molecular weight of less than or equal to 500 Daltons.

Gizurarson et al disclose a method for the topical administration of antigens and/or vaccines in mammals via a mucosal membrane. Gizurarson disclose that the antigen applied topically with polyoxyethylene sorbitan monomers enhances the immunological response following administration of the nasal, oral, rectal or vaginal passages. Gizurarson et al disclose that the composition may also include organic solvents such as benzyl alcohol and benzoic acid (page 9, lines 25-33), thus fulfilling the specific embodiments of claims 3, 7, 8, 11, 12-15 with respect to benzoic acid. Further, although Gizurarson et al do not specifically teach the further embodiments of claims 28-31 they would be inherent within the prior art method.

11. Claims 55 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by King et al (Vaccine, 1987, Vol. 5, pp. 234-238). The embodiments of claims 55 and 56 re recited above. King et al disclose a method for vaccinating a mammal against an antigen comprising delivering to the nasal passages a topically applied live vaccine.

12. Claims 1, 2, 12, 13, 14, 18, 27-31, 52 and 53 are rejected under 35 U.S.C. 102(e) as being anticipated by Glenn et al (U.S. 5,980,898). The specific embodiments of claims 1, 2, 12, 13, 14, 28-31 and 52 are recited above. Claim 18 embodies the method of claim 1 wherein the antigen is introduced into the mammal by a virus, bacterium, fungus or a parasite. Claim 27 embodies the method of claim 1 wherein the antigen is endogenous to the mammal and is pathologic. Claim 52 is drawn to a method for enhancing an immune response in a mammal against an endogenous antigen comprising repeated topical application to the mammal of a lipophilic compound having a molecular weight of less than or equal to 500 Daltons, wherein the lipophilic compound is applied in an amount sufficient to increase the number of antigen-bearing dendritic cells in a lymphoid organ. Claim 53 embodies the method of claim 52 wherein said endogenous antigen is a tumor antigen.

Glenn et al disclose a method for vaccinating a mammal comprising the administration of an antigen such as a tumor antigen (column 3, lines 64-67 and column 15, lines 52-67) in a composition comprising an activator of Langerhans cells, wherein said activators include trinitrochlorobenzene, dinitrofluorbenzene, pentadecylcatecol and lipid A (column 11, lines 31-40), thus fulfilling the specific embodiments of a lipophilic molecule having a molecular weight less than or equal to 500 Daltons. Glenn et al also disclose that the antigen may be derived from a pathogen that can infect the organism such as a bacterium, virus, fungus or parasite in addition to a autoantigen, thus fulfilling the specific embodiments of 18 and 27. Further, although Glenn et al do not specifically teach the further embodiments of claims 28-31 they would be inherent within the prior art method.

13. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Paul et al (Vaccine Research, 1995, Vol. 4, pp. 145-164) as evidenced by Roitt et al, (Immunology (text), 1993, pages 8.3-8.4). The specific embodiments of claim 1 are set forth above. Paul et al disclose a method for vaccinating a mammal against an antigen comprising the topical administration of an antigen encapsulated in tranfersomes. Paul et al disclose that the encapsulated protein traverses the stratum corneum by means of the ultradeformable submicroscopic transfersome vesicles

(page 147, fourth full paragraph). Paul does not specifically disclose that the number of antigen-bearing dendritic cells in a lymphoid organ are increased, however, that limitation would be inherent in the prior art method. Also, it is noted that Table 1 indicates that epicutaneous immunization with the transfersomes resulted in antic-BSA-FITC antibodies of the IgG2a isotype. This isotype is consistent with a TH1 response against the antigen and implies that activation of T-cells by antigen presenting cells substantiating the activation of dendritic cells (see Roitt et al, Immunology (text), 1993, pages 8.3-8.4).

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentable distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F. 3d 1428, 46 USPQ2d 1226 (Fed Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

15. Claims 1-3, 6-8, 11-16, 28-31, 51-57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,210,672. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '672 patent anticipate the instant claims.

16. Claims 17, 19-22 and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
February 24, 2003